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Letter to the editor: The use of an optimized colonoscopy protocol in a low-risk population for colorectal cancer prevention

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We read with interest the recent report from Xirasagar et al,¹ reporting a striking reduction in colorectal cancer (CRC) incidence and mortality with their optimized colonoscopy protocol. Using the South Carolina and US-SEER-18 populations as comparison groups, the authors computed that the expected number of CRC cases would be 104 over 78,375 person-years of observation. In contrast, only 18 cases were observed in patients enrolled in the colonoscopy-screening program. The 83% reduction in CRC incidence and 89% reduction in CRC mortality, were attributed to screening colonoscopies that used their protocol.

We do not dispute the benefit of colonoscopic screening and the importance of high quality examinations. However, the marked observed reduction in CRC is largely due to an inherent bias in study design, rather than improved screening. Estimation of the risk reduction due to a screening program entails following all patients who were enrolled, including those with asymptomatic CRC. People with asymptomatic CRC and large polyps are in the South Carolina and US-SEER-18 populations and so were included in the calculation of the “expected number” of CRC cases and deaths. Since they were excluded from the observed totals, what the authors actually computed was the standardized incidence ratio (SIR) of CRC incidence and mortality in the subset of screened patients who did not have asymptomatic CRC or large polyps. This is quite different than the SIR of CRC from the screening protocol itself.

The authors state “excluding cancer cases found at screening is essential, because the efficacy of screening colonoscopy represents future mortality reductions among screened beneficiaries who are protected from incident CRC by removal of premalignant lesions.” This statement is false, because removal of these asymptomatic CRC cases from the study cohort creates an imbalance of CRC risk at baseline between the groups. This is independent of the risk reduction due to polypectomy. If the 128 asymptomatic CRC cases were included in the study, the observed SIR would be 1.4 instead of 0.17. The risk is lowered further by excluding flat lesions, patients referred for surgical resection of an invasive polyp or obstructing mass, and those with incomplete colonoscopies.

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Thus, when using ad hoc registries like SEER to compare SIRs, it is important to make adjustments for asymptomatic cases of disease. While this method may not yield a true incidence, but rather a prevalence-incidence aggregate, the measure is standardized with comparison populations like SEER. For example, another study specifically addresses this problem by reporting the SIR of total CRC (including asymptomatic cases) and SIR after excluding these cases.² The difference in relative risk reduction in CRC incidence risk was 48% in the former group and 67% in the latter group. Similarly, trials investigating the reduction in CRC incidence associated with endoscopic screening and surveillance include asymptomatic cases of CRC in the study cohort.²⁻⁴ These studies have shown lower risk reductions ranging from 33-67%, than those reported by Xirasagar et al, and are more accurate estimates of the reduction in CRC incidence that can be expected from colonoscopic screening.

Furthermore, over two-thirds of the study cohort (69%) had no polyps on initial colonoscopy, a proportion within range of other colonoscopy studies in average risk persons.^{5,6} This group is known to be at low risk of CRC.⁷ Those with negative initial colonoscopies contribute to the low observed CRC risk, despite the fact that their low risk is not due to any of the procedural or operator factors emphasized in this article.

In summary, the study by Xirasagar et al demonstrated a decreased CRC incidence in their study cohort of patients with either negative index colonoscopies or low risk adenomas that were subsequently removed. This, in addition to the other exclusion criteria, created a study group at low risk for CRC. Thus, while the results were valid in estimating low CRC incidence and mortality in a group of screened patients, this risk reduction can largely be attributed to the composition of the study sample rather than the optimized colonoscopy screening protocol described. Of note, this methodological problem of excluding CRC cases found at index colonoscopy, when using similar comparison groups like SEER, is not unique to this one study and needs to be recognized.^{8,9}

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